



INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

国际药用菌学会

International Society for Medicinal Mushrooms (ISMM) was founded in Vancouver, Canada. As a global non-profit organization, ISMM promotes the development of research, education, production, transportation, marketing and cultivation of medicinal mushrooms to have people to work towards common aspirations and goals. The integration will increase the impact of the international medicinal mushroom industry and benefit the health of people in the world.

Honorable President: Prof. S.T.Chang, Prof.S.P. Wasser

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国际药用菌学会 (International Society for Medicinal Mushrooms), 简称ISMM, 在加拿大温哥华注册成立, 由从事药用菌产业的科研、教学、生产、流通、市场、文化及相关产业链的单位、团体和个人自愿组成的为实现共同意愿的非营利性国际组织。本学会致力于促进国际药用菌产业各个领域的融合与发展, 以提升药用菌行业在全球的影响力, 造福人类健康。

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NEWSLETTER OF THE INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

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Call for Papers

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News Reports

How A Humble Mushroom could Save Forests and Fight Climate Change

By Paul W Thomas



The blue milk cap mushroom is a rich source of protein. laerke_lyhne, CC BY-SA

The conversion of forests to agricultural land is happening at a mind-boggling speed. Between 2015 and 2020, the rate of deforestation was estimated at around 10 million hectares every year.

Compared to 2012, the UN's Food and Agriculture Organisation (FAO) is predicting a massive increase in agricultural demand of 50% by 2050. In South America, around 71% of rainforest has been replaced by pasture and a further 14% has been lost to the production of animal feed. One of the key successes of COP26 was a pledge from world leaders to end deforestation by 2030.

From a climate and carbon point of view, we know that cutting down trees at this scale is devastating. But the impacts run deeper: 75% of the world's accessible fresh water arises from forested watersheds. And with 80% of the world's population facing a threat to their water security, trees play a very significant role in stemming desertification and preventing soil erosion. They also protect against flooding in coastal areas as well as being home to a huge number of species, many of which are important crop pollinators.

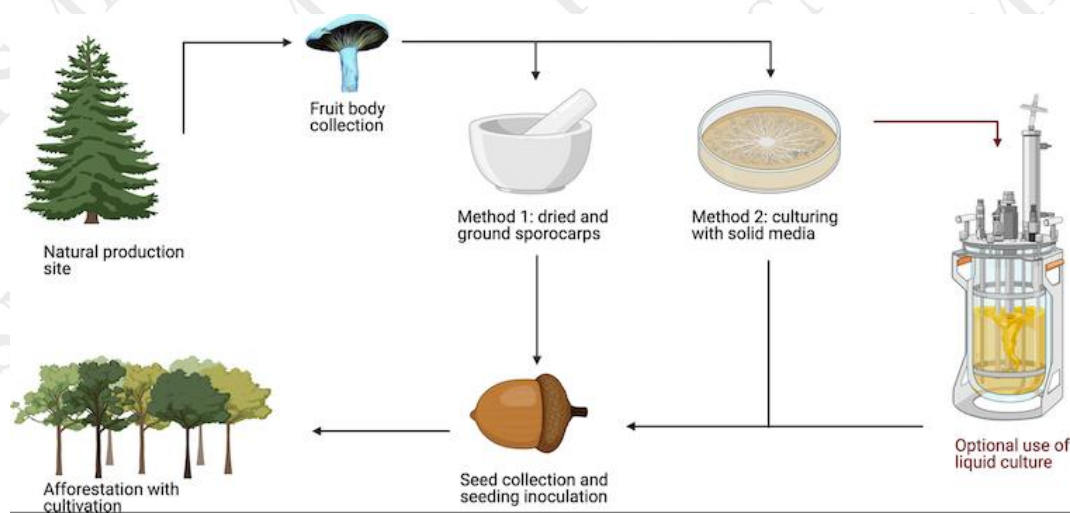
So what can we do? We know that different foods have different footprints. Reducing the quantity of animal-based products will have a huge impact. In fact, eating less meat is one of the most potent changes that people in the west can make to help save the planet.

But what if we could go further? What if, instead of having farming and forestry in direct conflict, we could develop a system that allows food production and forest on the same parcel of land?

Miraculous mushrooms

This is exactly what our latest research focuses on, looking at fungi that grow in partnership with trees, in a mutually beneficial arrangement. This is a common association and some species can produce large mushroom fruiting bodies, such as the highly prized truffle. Aside from this delicacy, cultivation of these species is a new and emerging field. But progress is especially being made in one group known as milk caps, that include a beautiful and unusually bright blue species known as *Lactarius indigo*, or the blue milk cap.

High in dietary fibre and essential fatty acids, this edible mushroom's blue pigmentation means they are easy to identify safely. With extracts demonstrating antibacterial properties and an ability to kill cancer cells, the blue milk cap could also be a source of pharmacological potential.



Paul Thomas/University of Stirling, Author provided

In our paper, we describe how to cultivate this species, from isolation in the lab to creating young tree saplings with roots inoculated with this symbiotic fungus. These trees can then be planted at scale in suitable climate zones ranging from Costa Rica to the US. As the tree and fungus's partnership matures, they start to produce these incredible mushrooms packed with protein.

The agriculture on cleared forested land is dominated by pastoral beef production where around 4.76-6.99kg of protein per hectare per year is produced. But, if this system was replaced with planting trees hosting the milk cap fungus, the same parcel of land could produce 7.31kg of protein every year. The mushrooms can be consumed fresh, processed or the protein content can be extracted to produce other food items.

This would lead to more food production, with all the benefits forests bring and without the environmental burdens of intensive farming such as fertiliser, water use or the growing of additional feed. Beef farming contributes to climate change by emitting greenhouse gases, but as these fungus-inoculated trees grow, they draw down carbon from the atmosphere, helping in our fight against the climate crisis. So, as well as producing more food, the process can also

enhance biodiversity, aid conservation, act as a carbon sink for greenhouse gases and help stimulate economic development in rural areas.



Forests are still being bulldozed to make way for agricultural land for beef production. Richard Whitcombe/Shutterstock

In Mexico, harvesting is often a family activity where fungi are traded informally or exchanged for goods and in neighbouring Guatemala, the blue milk cap is listed as one of the most popular edible mushrooms. So there is economic potential and community empowerment at a smaller local scale as well as trading opportunities for national and international corporations.

We believe this approach is cheaper – or more cost effective – than beef farming. But this is a new technology and like all new innovations, support is needed. This means further research and proper financial investment to develop the technology to a point where agribusinesses feel confident to invest at scale.

But even with support, there must also be demand for the end product. Doubtless with health and environmental concerns in mind, the proportion of meat eaters who have reduced or limited the amount of meat they consume has risen from 28% in 2017 to 39% in 2019, according to market research. And sales of meat-free foods are expected to reach £1.1 billion by 2024. Clearly there's a market, as ordinary people endeavour to do their bit for the planet. With so much at stake we must urgently pursue the promising options that fungi provide.

Source: <https://theconversation.com/>

The 11th International Medicinal Mushroom Conference Held in Belgrade

The 11th International Medicinal Mushroom Conference held on September 27-30 in Belgrade. After several postponements due to Covid, the 11th IMMC Congress was organized in the Crown Plaza Hotel in Belgrade, Serbia. 180 participants from 50 countries were present. More participation was expected, but due to the complex international situation (conflict in Eastern Europe and hygiene problems in China), a large part of registered guests, especially from China, could not participate. It was the first hybrid conference where we listened to several lectures in the form of a video conference.



In addition, for the first time, the conference was made available via the Internet to other, especially foreign, participants. A number of traditional speakers were absent from the conference, but a number of new faces from new scientific workplaces appeared among the speakers and in the audience. It was pleasant to notice how the auditorium and the lecturers have become younger.



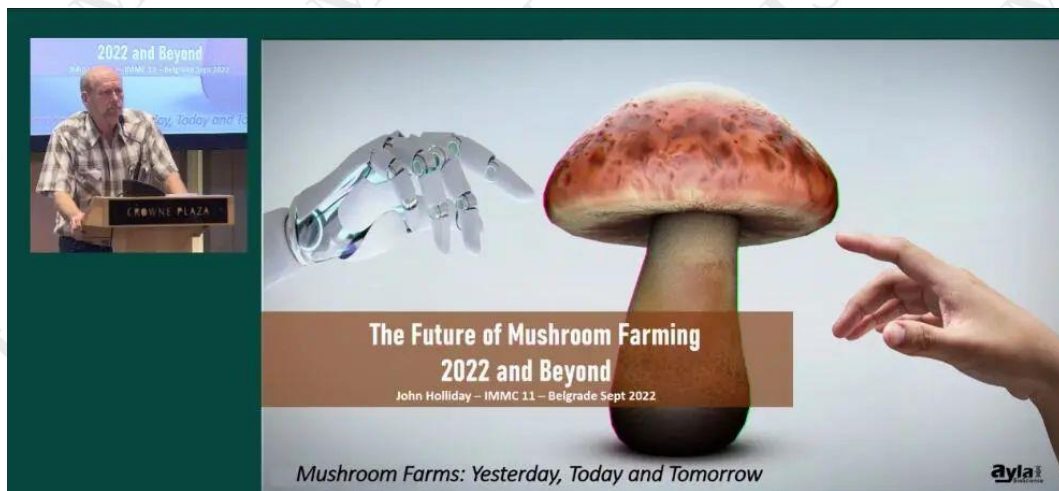
Prof. Miomir Nikšić, President of the IMMC11 Organizing Committee, addressed on Opening Ceremony



Prof. Li Yu, President of International Society for Medicinal Mushrooms (ISMM), addressed on the Opening Ceremony

The theme of the conference: Medicinal Mushroom Science: Innovation, Challenges and Perspectives, with 9 key topics including medicinal mushrooms biodiversity, genetics and breeding, cultivation, biochemistry and pharmacology,

nutritional and medicinal value, products, used in veterinary and agriculture, in clinical practice, as well as the Psychedelic Mushrooms.



Prof. John Holliday gave a speech on the conference

85 keynote lectures, plenary and invited lectures were given and 47 posters were presented. The posters were presented in the form of short personal messages. All lectures were recorded on video and will be accessible in electronic form. The conference ended with a visit to the mushroom exhibition in the Botanical garden in Belgrade where 240 different species of fungi were presented.



Finally, thanks must be expressed to the all organizing committee under the leadership of Prof. Miomir Nikšić for having managed to organize the conference, so perfectly.

The next 12th ICMM conference will be held in September 2024 in Bari, Italy.

Up-coming Events

The 10th International Conference on Mushroom Biology and Mushroom Products (10th

ICMBMP)



ORGANIZED BY:



CO-ORGANIZED BY:



SCIENTIFIC PROGRAM:

The 10th ICMBMP will feature the latest advances in topics relating to all aspects of mushroom biology and mushroom products as keynote, plenary, oral and poster presentations in following tracks:

- Mushroom Biology

- Mushrooms: Nutritional and Medicinal Properties
- Mushroom Cultivation: Innovation and Management
- Pest and Disease Management
- Mushroom Product Quality and Safety Controls
- Mushroom in Healthy Environment
- Mushroom Economics and Cultural Impacts

ABSTRACT SUBMISSION

The author is recommended to use this template to prepare the abstract. The A4 paper size (21cm x 29.7cm) and the margin settings are: Top & Bottom & Left & Right - 2.5cm. Type abstract using 11-point Times New Roman, single spacing and justified. The one-page abstract should briefly state the aims, the main results, and the conclusions in maximum 250 words. Do not include references.

REGISTRATION FEES

Online	Participants*		students**	
	International	Malaysian	International	Malaysian
*Rate perday	USD 25	RM 50	USD 15	RM 40
Full package	USD 70	RM 150	USD 50	RM 100
Physical				
*Rate perday	USD 50	RM 100	USD 25	RM 60
Full package	USD 150	RM 280	USD 100	RM 200

*Researchers, Academics, Industry; ** Valid Proof of StudentStatus; *if daily attendance do calculate fees based on numberof attendance days (full package includes post conferenceactivities on Day 4).

METHOD OF PAYMENT

Do register using google formand attached the proof of payment OR email completed PDF format registration form together with the proof of payment to icmbmp2022@gmail.com.

***ALL DIRECT BANK TRANSFERS OF REGISTRATION FEES SHOULD INCLUDE THE BANK CHARGES**

IMPORTANT DATES & DEADLINES

- Registration Open: 15 Sept 2022
- Abstract Deadline: 31 Jan 2023
- Registration Close: 15 Feb 2023

CONTACT

Mushroom Research Centre Universiti Malaya (MRCUM)

Tel: +603-79676703; E-mail: icmbmp2022@gmail.com

The Dutch Mushroom Days 2023



10-12 May 2023, De Brabanthallen, 's-Hertogenbosch

The Dutch mushroom industry is well known and one of the biggest players in the mushroom industry worldwide! The Mushroom Days is the perfect platform for National and International companies to present their technologies and services and to get the latest information and insights from the international industry. This event is the platform to meet all relevant mushroom growers and related industry players.

The Dutch Mushroom Days, originally planned to take place from July 6-8, 2022, has been moved to **May 10-12, 2023**.

Why Participate

The Mushroom Days

This platform gives you the opportunity to meet all relevant mushroom growers and related players in the industry. The Mushroom Days are an indispensable part of your marketing and sales strategy.

During the Mushroom Days you can:

- Meet and inspire industry professionals
- Expand your network
- Introduce new products and / or services
- Build brand awareness
- Achieve direct sales
- Benefit from a broad international promotional campaign
- Get high returns on your investment
- Overload your organization with new impressions

Location & Opening hours

Date	Event	Time
Wednesday 10 May 2023	Exhibition	10.00 – 17.00 hrs
	Welcome Event	17.00 – 21.00 hrs
Thursday 11 May 2023	Exhibition	10.00 – 18.00 hrs
Friday 12 May 2023	Exhibition	10.00 – 17.00 hrs

Location

Brabanthallen, Diezekade 2, 5222 AK, 's-Hertogenbosch, The Netherlands

Contact

For more information, please contact the project team

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Email: info@champignondagen.nl

Source: www.champignondagen.nl

2023 International Mushroom Days

In light of the continuing pandemic and ongoing group gathering and travel restrictions, the organization committee of International Mushroom Days had made the decision to postpone the 2022 International Mushroom Days to March 18-20, 2023, in Xiamen Fliport C&E Center, China.

2023 International Mushroom days will be hosted by China Chamber of Commerce of I/E of Foodstuffs, Native Produce and Animal By-products (CFNA), organized by Xiamen Vissea Exhibition Service Co., LTD., Xiamen Wutong Fliport Hotel and Xiamen Fliport C&E Center. The Expo will help rural revitalization, promote innovation and development of the whole industrial chain of Chinese mushroom, promote the integration of domestic and foreign trade, all-channel layout and sustainable development, and the high-quality products of the whole industrial chain of mushroom at home and abroad in the post-epidemic era.



Xiamen Wutong Fliport Hotel and Xiamen Fliport C&E Center

As an upgraded version of the 2020 International Mushroom Days (Xiamen), the new Expo with an extended scale will occupy the first and second floor exhibition halls of Xiamen Fliport C&E Center. The organizing committee will pay more attention to the effective combination of the conference and exhibition, and make use of the space advantages to create an integrated exhibition. The first floor of the exhibition hall will be used as the Intelligent Manufacturing and Innovative Pavilion of Mushroom, which will display various equipment and supporting facilities, including raw and auxiliary materials, production, sterilization, inoculation, environmental simulation, packaging and processing. On the second floor, a mushroom industry revitalization hall will be set up to display the achievements of rural revitalization and the style of premium edible mushroom brand enterprises. The total scale of the Expo will be 15,000 square meters with about 600 international standard booths.

Contact mail: imd_info@163.com.

20th ISMS Congress & 26th NAMC

20th ISMS Congress and 26th NAMC 26-29 February 2024, Las Vegas, USA



The dates and venue for the 20th International Congress on the Science and Cultivation of Edible and Medicinal Mushrooms organized by ISMS have been set.

This long-awaited event will be held in conjunction with the 26th North American Mushroom Conference at the JW Marriot Las Vegas Resort & Spa <https://www.marriott.com/en-us/hotels/lasjw-jw-marriott-las-vegas-resort-and-spa/overview/> in Las Vegas, Nevada in the USA from 26 – 29th February 2024.

Pls save the dates in your calendar. February 2024 seems a long way off, but time is flying by. ISMS and AMI began planning for the event some time ago so you can expect updates over the next 15 months as key pieces of planning become reality. If you have any immediate questions, please email them to secretariat@isms.biz.

Calls for ISMS abstract submissions will begin early in 2023. Authors and presenters can expect a similar format and process that was used for the ISMS e-Congress last year.

A detailed email on abstract requirements and process, and presentation guidelines for Las Vegas will be sent out in December.

By the time we get to Las Vegas it will be almost 8 years since we last got together as an ISMS family. I sense the 20th ISMS Congress will be one event you will not want to miss.

Greg Seymour

President, ISMS



The 12th International Medicinal Mushrooms Conference (IMMC12)

The 12th International Medicinal Mushrooms Conference to be organized in Bari, Italy, from Sept. 24 to 27, 2024, by Prof. Maria Letizia Gargano (marialetizia.gargano@uniba.it) of the Department of Soil, Plant, and Food Sciences of the University "Aldo Moro" of Bari and Prof. Giuseppe Venturella (University of Palermo, giuseppe.venturella@unipa.it) in the role of President of the Italian Medicinal Mushrooms Society (SIFM). The website will be open soon and the venue for IMMC12 is The Nicolaus Hotel Bari (<https://www.thenicolaushotel.com/hotel/concept/>).



The Organizing Committee invites you to attend

IMMC 12

September 24 - 27, 2024

BARI, ITALY

Save the date



After Kiev, Ukraine in 2001; Pattaya, Thailand in 2003; Port Townsend, USA in 2005; Ljubljana, Slovenia in 2007; Nantong, China in 2009; Zagreb, Croatia in 2011; Beijing, China in 2013; Manizales, Colombia in 2015; Palermo, Italy in 2017; Nantong, China in 2019 and Belgrade, Serbia in 2020, the **IMMC 12** The International Medicinal Mushrooms Conference will be held in **Bari** from 24 - 27 of September 2024 organized by the **University of Bari "Aldo Moro"** and by the **Italian Society for Medicinal Mushrooms (SIFM)**.



Web site will open in January 2023.

First circular will be distributed in March-April 2023.

Registration will begin in August 2023.

After publishing the first circular, abstracts can be submitted until the end of February 2024.



Research progress

Antiviral Bioactive Compounds of Mushrooms and Their Antiviral Mechanisms: A Review

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Abstract: Mushrooms are used in their natural form as a food supplement and food additive. In addition, several bioactive compounds beneficial for human health have been derived from mushrooms. Among them, polysaccharides, carbohydrate-binding protein, peptides, proteins, enzymes, polyphenols, triterpenes, triterpenoids, and several other compounds exert antiviral activity against DNA and RNA viruses. Their antiviral targets were mostly virus entry, viral genome replication, viral proteins, and cellular proteins and influenced immune modulation, which was evaluated through pre-, simultaneous-, co-, and post-treatment in vitro and in vivo studies. In particular, they treated and relieved the viral diseases caused by herpes simplex virus, influenza virus, and human immunodeficiency virus (HIV). Some mushroom compounds that act against HIV, influenza A virus, and hepatitis C virus showed antiviral effects comparable to those of antiviral drugs. Therefore, bioactive compounds from mushrooms could be candidates for treating viral infections.

Keywords: mushroom, bioactive compound, virus, infection, antiviral mechanism

Viruses **2021**, *13*, 350, <https://doi.org/10.3390/v13020350>

Application of Identification and Evaluation Techniques for Edible Mushrooms: A Review

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²*Zhaotong University, Zhaotong, China;*

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Abstract: Edible mushrooms are healthy food with high nutritional value, which is popular with consumers. With the increase of the problem of mushrooms being confused with the real and pollution in the market, people pay more and more attention to food safety. More than 167 articles of edible mushroom published in the past 20 years were reviewed

in this paper. The analysis tools and data analysis methods of identification and quality evaluation of edible mushroom species, origin, mineral elements were reviewed. Five techniques for identification and evaluation of edible mushrooms were introduced and summarized. The macroscopic, microscopic and molecular identification techniques can be used to identify species. Chromatography, spectroscopy technology combined with chemometrics can be used for qualitative and quantitative study of mushroom and evaluation of mushroom quality. In addition, multiple supervised pattern-recognition techniques have good classification ability. Deep learning is more and more widely used in edible mushroom, which shows its advantages in image recognition and prediction. These techniques and analytical methods can provide strong support and guarantee for the identification and evaluation of mushroom, which is of great significance to the development and utilization of edible mushroom.

Keywords: Chromatography, deep learning, edible mushroom, quality evaluation, spectroscopic

Critical Reviews in Analytical Chemistry, <https://doi.org/10.1080/10408347.2021.1969886>

Ten decadal advances in fungal biology leading towards human well-being

Ausana Mapook¹, Kevin D. Hyde^{1,2,17,19,20,23}, Khadija Hassan³, Blondelle Matio Kemkuignou³, Adéla Čmoková⁵, Frank Surup^{3,4}, Eric Kuhnert⁶, Pathompong Paomephan^{3,7}, Tian Cheng^{3,5}, Sybren de Hoog^{8,9,10}, Yinggai Song¹¹, Ruvishika S. Jayawardena^{1,2}, Abdullah M. S. Al-Hatmi^{8,12}, Tokameh Mahmoudi¹³, Nadia Ponts¹⁴, Lena Studt-Reinhold¹⁵, Florence Richard-Forget¹⁴, K. W. Thilini Chethana^{1,2}, Dulanjalee L. Harishchandra^{1,2,16}, Peter E. Mortimer^{17,18}, Huili Li^{17,18}, Saisamorn Lumyong^{19,20,21}, Worawoot Aiduang²⁰, Jaturong Kumla^{19,20}, Nakarin Suwannarach^{19,20}, Chitrabhanu S. Bhunjun^{1,2}, Feng-Ming Yu^{1,2,22}, Qi Zhao²², Doug Schaefer¹⁸ & Marc Stadler^{3,4}

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Abstract: Fungi are an understudied resource possessing huge potential for developing products that can greatly improve human well-being. In the current paper, we highlight some important discoveries and developments in applied mycology and interdisciplinary Life Science research. These examples concern recently introduced drugs for the treatment of infections and neurological diseases; application of –OMICS techniques and genetic tools in medical mycology and the regulation of mycotoxin production; as well as some highlights of mushroom cultivation in Asia. Examples for new diagnostic tools in medical mycology and the exploitation of new candidates for therapeutic drugs, are also given. In addition, two entries illustrating the latest developments in the use of fungi for biodegradation and fungal biomaterial production are provided. Some other areas where there have been and/or will be significant developments are also included. It is our hope that this paper will help realise the importance of fungi as a potential industrial resource and see the next two decades bring forward many new fungal and fungus-derived products.

Keywords: biomaterial, CRISPR, drug development, morel cultivation, mushroom cultivation, mycotoxin biosynthesis, plastic degradation

Fungal Diversity (2022) 116:547–614; <https://doi.org/10.1007/s13225-022-00510-3>

Fungal taxonomy: current status and research agendas for the interdisciplinary and globalisation era

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Abstract: Fungal taxonomy is a fundamental discipline that aims to recognise all fungi and their kinships. Approximately 5% of a practical estimate of 2.2–3.8 million species globally are currently known, and consequently the Fungal Tree of

Life (FTOL) is very incompletely reconstructed. With the advances of new technologies, mycology is marching into the interdisciplinary and globalisation era. To make fungal taxonomy relevant, innovative sampling methods and phylogenomics analyses should be performed to reconstruct a much more comprehensive FTOL. In association with this densely sampled FTOL, multiomics will reveal what drives fungal species diversification and how fungal traits evolve to adapt to various environments, while metagenomics will facilitate the understanding and protection of the ecological functions of fungi. A coordinated approach to pursuing these research agendas that includes conceiving of and costing a mission to describe all the fungi on the planet will unlock potential of fungi to support sustainable development of our society.

Keywords: coordination, ecology and conservation, evolutionary biology, fungal resources, fungal tree of life

Mycology, DOI:10.1080/21501203.2022.2103194

Cordyceps mushroom with increased cordycepin content by the cultivation on edible insects

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Abstract: Cordycepin is the major constituent of *Cordyceps* mushroom (or *Cordyceps militaris*) with therapeutic potential. Insects are the direct sources of nutrients for *Cordyceps* in nature. Therefore, optimized condition of *Cordyceps* cultivation for efficient cordycepin production was explored using six edible insects as substrates. The highest yield of cordycepin was produced by the cultivation on *Allomyrina dichotoma* and was 34 times that on *Bombyx mori* pupae. Among insect components, fat content was found to be important for cordycepin production. Especially, a positive correlation was deduced between oleic acid content and cordycepin production. The transcriptional levels of *cns1* and *cns2*, genes involved in cordycepin biosynthesis, were higher in *Cordyceps* grown on *A. dichotoma* than on other insects tested. The addition of oleic acid to the substrates increased cordycepin production together with the transcriptional levels of *cns1* and *cns2*. Therefore, *Cordyceps* with high content of cordycepin can be secured by the cultivation on insects.

Keywords: *Cordyceps militaris*, cordycepin, *Allomyrina dichotoma*, oleic acid, *cns1* and *cns2*

Front. Microbiol., 19 October 2022 Sec. Microbiotechnology <https://doi.org/10.3389/fmicb.2022.1017576>

Metabolites and Their Bioactivities from the Genus Cordyceps

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Abstract: The *Cordyceps* genus is a group of ascomycete parasitic fungi, and all known species of this genus are endoparasites; they mainly feed on insects or arthropods and a few feed on other fungi. Fungi of this genus have evolved highly specific and complex mechanisms to escape their host's immune system and coordinate their life cycle coefficients with those of their hosts for survival and reproduction; this mechanism has led to the production of distinctive metabolites in response to the host's defenses. Herein, we review approximately 131 metabolites discovered in the genus *Cordyceps* (including mycelium, fruiting bodies and fungal complexes) in the past 15 years, which can be used as an important source for new drug research and development. We summarize chemical structures, bioactivity and the potential application of these natural metabolites. We have excluded some reports that originally belonged to *Cordyceps*, but whose taxonomic attribution is no longer the *Cordyceps* genus. This can and will serve as a resource for drug discovery.

Keywords: *Cordyceps*; *Cordyceps sinensis*; metabolites; bioactivity

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Fermentation characteristics and flavor properties of *Hericium erinaceus* and *Tremella fuciformis* fermented beverage

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Abstract: This study evaluated and compared the fermentative and flavor properties of *Hericium erinaceus* and *Tremella fuciformis* fermented beverage (HTFB) produced by four commercial lactic acid bacteria (LAB), i.e., *L. plantarum*, *L. rhamnosus*, *L. paracasei* or *S. thermophilus*. All four strains showed the probiotic potential of utilizing *Hericium erinaceus* and *Tremella fuciformis* as fermentation substrates. Among four LAB, *L. plantarum* produced significantly highest concentrations of total acids (76.16 g/L), while the viable count of HTFB inoculated with *L. paracasei* was the highest (7.18 log CFU/mL). The contents of bioactive components such as polyphenols and triterpenoids significantly increased after fermentation regardless of the strains. The fermentation process enriched the volatile profile and reduced the unpleasant flavors such as nonanal and 1-octen-3-ol. According to the relative odor activity values and PLS-DA analysis, a total of 8 volatile organic compounds were identified as markers with odor contributions. Furthermore, the olfactory characteristics of the four beverages could be clearly distinguished by electronic nose. The electronic tongue results showed that the fermentation process increased the sourness and decreased the bitterness and astringency of the beverage, resulting in an improved taste property. The sensory evaluation finally confirmed that HTFB inoculated with *L. paracasei* was the most acceptable product to consumers with high overall flavor coordination. Overall, this work provided valuable information for the selection of premium fermentation strains to produce fermented edible fungi beverages with better nutritional and sensory qualities.

Keywords: *Hericium erinaceus*, *Tremella fuciformis*, lactic acid bacteria, fermentation, volatile compounds, relative odor activity value

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Secrets of Flavonoid Synthesis in Mushroom Cells

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Abstract: Flavonoids are chemical compounds that occur widely across the plant kingdom. They are considered valuable food additives with pro-health properties, and their sources have also been identified in other kingdoms. Especially interesting is the ability of edible mushrooms to synthesize flavonoids. Mushrooms are usually defined as a group of fungal species capable of producing macroscopic fruiting bodies, and there are many articles considering the content of flavonoids in this group of fungi. Whereas the synthesis of flavonoids was revealed in mycelial cells, the ability of mushroom fruiting bodies to produce flavonoids does not seem to be clearly resolved. This article, as an overview of the latest key scientific findings on flavonoids in mushrooms, outlines and organizes the current state of knowledge on the ability of mushroom fruiting bodies to synthesize this important group of compounds for vital processes. Putting the puzzle of the current state of knowledge on flavonoid biosynthesis in mushroom cells together, we propose a universal scheme of studies to unambiguously decide whether the fruiting bodies of individual mushrooms are capable of synthesizing flavonoids.

Keywords: mushrooms; fruiting bodies; mycelia; flavonoids; biosynthesis; HPLC; gene expression; metabolites

Cells **2022**, *11*(19), 3052; <https://doi.org/10.3390/cells11193052>

Potential of antitumor activity by antibody drugs and mushroom-derived β -glucans in natural killer cell-mediated tumoricidal activities against non-Hodgkin's B-cell lymphoma

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Abstract: β -glucans are polysaccharides that activate innate immunity. We herein investigated whether β -glucans promote the immunological effects of antibody drugs against malignant tumor cells using human peripheral blood mononuclear cells (PBMCs). Rituximab bound to CD20-specific lymphoma and exhibited cytotoxic activity in the presence of human mononuclear cells, but not neutrophils. The addition of Hanabiratake (cauliflower mushroom)-derived β -glucan (SCG) and granulocyte-macrophage colony-stimulating factor (GM-CSF) to co-cultures of PBMCs and Raji lymphoma cells further promoted antibody-dependent cell-mediated cytotoxicity (ADCC). The GM-CSF treatment increased β -glucan receptor expression on adherent cells in PBMCs. A co-stimulation with GM-CSF and SCG of PBMCs induced an increase in the number of spreading cells and the activation of natural killer (NK) cells. The enhancement in ADCC was abolished by the removal of NK cells, indicating that SCG and GM-CSF increased ADCC against lymphoma by activating β -glucan receptor-expressing cells in PBMCs and enhancing NK cell activity. The synergistic mechanisms of action of mushroom-derived β -glucans and biopharmaceuticals, including recombinant cytokines and antibodies, in the treatment of malignant tumor cells provide important insights into the clinical efficacy of β -glucans from mushrooms.

Mushrooms as future generation healthy foods

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Abstract: The potential of edible mushrooms as an unexploited treasure trove, although rarely included in known food guidelines, is highlighted. Their role in shielding people against the side effects of an unhealthy stylish diet is reviewed. Mushrooms complement the human diet with various bioactive molecules not identified or deficient in foodstuffs of plant and animal sources, being considered a functional food for the prevention of several human diseases. Mushrooms have been widely used as medicinal products for more than 2,000 years, but globally the potential field of use of wild mushrooms has been untapped. There is a broad range of edible mushrooms which remain poorly identified or even unreported which is a valuable pool as sources of bioactive compounds for biopharma utilization and new dietary supplements. Some unique elements of mushrooms and their role in preventative healthcare are emphasized, through their positive impact on the immune system. The potential of mushrooms as antiviral, anti-inflammatory, anti-neoplastic, and other health concerns is discussed. Mushrooms incorporate top sources of non-digestible oligosaccharides, and ergothioneine, which humans are unable to synthesize, the later a unique antioxidant, cytoprotective, and anti-inflammatory element, with therapeutic potential, approved by world food agencies. The prebiotic activity of mushrooms beneficially affects gut homeostasis performance and the balance of gut microbiota is enhanced. Several recent studies on neurological impact and contribution to the growth of nerve and brain cells are mentioned. Indeed, mushrooms as functional foods' nutraceuticals are presently regarded as next-generation foods, supporting health and wellness, and are promising prophylactic or therapeutic agents.

Keywords: fungi nourishment, bioactive elements, healthcare prevention, functional foods, pharmanutrients

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International Journal of Medicinal Mushrooms Call for Papers

About *International Journal of Medicinal Mushrooms*

International Journal of Medicinal Mushrooms is a journal covering the technologies/fields/categories related to Applied Microbiology and Biotechnology (Q3); Drug Discovery (Q3); Pharmacology (Q3). It is published by Begell House Inc.. The overall rank of *International Journal of Medicinal Mushrooms* is 10594. According to SCImago Journal Rank (SJR), this journal is ranked 0.471. SCImago Journal Rank is an indicator, which measures the scientific influence of journals. It considers the number of citations received by a journal and the importance of the journals from where these citations come. SJR acts as an alternative to the Journal Impact Factor (or an average number of citations received in last 2 years). This journal has an h-index of 30. The best quartile for this journal is Q3.

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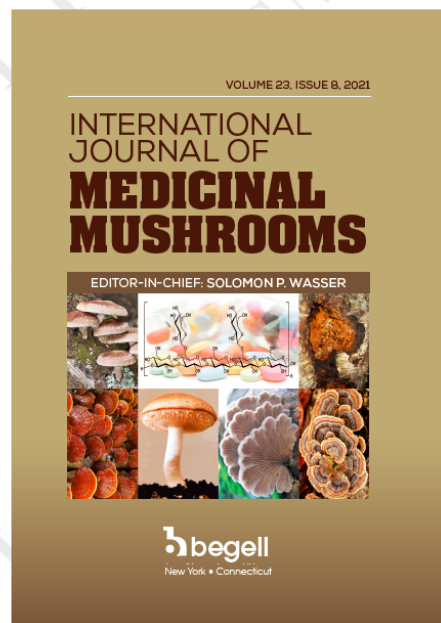
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Aims and Scope

The rapid growth of interest in medicinal mushrooms research is matched by the large number of disparate groups that currently publish in a wide range of publications. The *International Journal of Medicinal Mushrooms* is the one source of information that will draw together all aspects of this exciting and expanding field - a source that will keep you up to date with the latest issues and practice. The *International Journal of Medicinal Mushrooms* publishes original research articles and critical reviews on a broad range of subjects pertaining to medicinal mushrooms, including systematics, nomenclature, taxonomy, morphology, medicinal value, biotechnology, and much more. Papers on new techniques that might promote experimental progress in the aforementioned field are also welcomed. In addition to full-length reports of original research, the journal publishes short communications and interesting case reports, together with literature reviews. Letters to the editor on topics of interest to readers are also published.

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International Journal of Medicinal Mushrooms

2023, Vol. 25, Issue no.1

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International Journal of Medicinal Mushrooms

2023, Vol. 25, Issue no.3

Potential of Antitumor Activity by Antibody Drugs and Mushroom-derived β -glucans in Natural Killer Cell-mediated Tumorcidal Activities Against non-Hodgkin's B-cell Lymphoma

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Points and Reviews

Mycochemicals in Wild and Cultivated Mushrooms: Nutrition and Health

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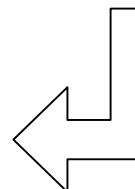
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Abstract: The mushrooms have contributed to the development of active ingredients of fundamental importance in the field of pharmaceutical chemistry as well as of important tools in human and animal health, nutrition, and functional food. This review considers studies on the beneficial effects of medicinal mushrooms on the nutrition and health of humans and farm animals. An overview of the chemical structure and composition of mycochemicals is presented in this review with particular reference to phenolic compounds, triterpenoids and sterols, fatty acids and lipids, polysaccharides, proteins, peptides, and lectins. The nutritional value and chemical composition of wild and cultivated mushrooms in Italy is also the subject of this review which also deals with mushrooms as nutraceuticals and the use of mushrooms in functional foods. The nutraceutical benefits of UV irradiation of cultivated species of basidiomycetes to generate high amounts of vitamin D2 is also highlighted and the ability of the mushrooms to inhibit glycation is analyzed. Finally, attention is paid to studies on bioactivities of some Italian wild and cultivated mushrooms with particular reference to species belonging to the genus *Pleurotus*. The review highlights the potential of medicinal mushrooms in the production of mycochemicals that represent a source of drugs, nutraceutical, and functional food.

Graphic abstract



Sample	Molecular Weight (kDa)	Monosaccharide Composition (%) ^a						
		Glc	Rham	Gal	Xyl	Ara	Man	Fru
PEPS-A	—	94.8	— ^b	—	—	—	5.2	—
PEPS-B	—	60.8	—	—	—	—	3.0	36.2
PEPS-A1	68	100	—	—	—	—	—	—
PEPS-A2	43	100	—	—	—	—	—	—

^aIndividual components were identified by comparison with standard sugars.

^bNot detected.

Keywords: Fungal diversity, Cultivation, Mycochemicals, Chemical structures, Nutrition

Abbreviations

AGLs	Acidic glycosphingolipids
BEPP	<i>Boletus edulis</i> Polysaccharides
BRMs	Biological response modifiers
CBAEP	Cibacron blue affinity-purified protein
COSY	Correlation spectroscopy
FAB-MS	Fast atom bombardment
FAME	Fatty acid methyl esters
FIP	Immunomodulatory proteins
FT-IR	Fourier-transformed infrared spectroscopy
GC	Gas chromatography
GLC-MS	Gas-liquid chromatography-mass spectrometry
GLS	Glycosphingolipids
GSH	Glutathione peroxidase
HBA	Hydroxybenzoic acid
HCA	Hydroxycinnamic acid
HIV	Human immunodeficiency viruses
HMBC	Heteronuclear multiple bond coherence
HMG-CoA	β -Hydroxy β -methylglutaryl-CoA
HMQC	Heteronuclear multiple quantum coherence
HPLC-MS	Liquid chromatography-mass spectrometry
HS-ITEX	Head Space "In Tube Extraction"
GC-MS	Technique and gas chromatography
IEC	Ion-exchange chromatography
iNKT	Invariant natural killer cell
LCB	Long-chain base
LDG-M	<i>Lactarius deliciosus</i> Polysaccharides

MHS-SPME	Multiple headspace-solid phase microextraction
MIC	Minimum inhibitory concentration
MM	Medicinal mushrooms
MUFA	Monounsaturated fatty acid
NMR	Nuclear magnetic resonance
NOESY	Nuclear overhauser effect spectroscopy
OMW	Olive mill wastewaters
PELPS	<i>Pleurotus eryngii</i> var. <i>elaeoselini</i> polysaccharides
PEPE	<i>Pleurotus eryngii</i> Purified polysaccharides
PSK	Polysaccharide K
PSP	Polysaccharide peptide
PUFA	Polyunsaturated fatty acid
ROESY	Rotating-frame nuclear overhauser effect correlation spectroscopy
RVP	<i>Russula virescens</i> Polysaccharide
SEC	Size-exclusion chromatography
SFA	Saturated fatty acid
SPG	Schizophyllan
TLC	Thin layer chromatography
TOCSY	Total correlation spectroscopy
TPC	Total phenolic content
VOC	Volatile organic compounds

Introduction

Definition of mycochemicals

For millennia, mushrooms were well known as a nutritional and pharmaceutical resource especially in traditional oriental therapies, but after the discovery of Penicillin (Fleming [1929](#)), they became a prominent source of natural antibiotics and other bioactive compounds.

The subject of mycochemistry, has developed as a distinct discipline that is concerned with the enormous variety of chemical substances, named “mycochemicals”, elaborated and accumulated by mushrooms. It deals with the isolation and structure elucidation of the chemical structures of these substances, their biosynthesis, metabolism, turnover, their natural distribution, and their biological properties (Dewick [2009](#)).

The mycochemicals play an important role in human and animals health, nutrition, and as functional food (Scheme [1](#)).

Obviously, in all these applications, methods are needed for separation, and identification of the many different mycochemicals present in mushrooms. Thus, advances in our understanding of mycochemistry are directly related to the application of known techniques together with the continuing development of new analytical techniques to solve outstanding problems as they appear (Ruthes et al. [2015](#)).

The characterization of mycochemicals is carried out using one or other, or a combination, of different chromatographic

techniques that include thin layer chromatography (TLC), gas and/or liquid chromatography (CC, GC, HPLC). FT-IR, mass spectrometry and NMR experiments [$1D\ ^1H$, ^{13}C NMR and 2D NMR ($H-H$ COSY, TOCSY, HMQC, HMBC and NOESY)] are useful in providing information for the mycochemical structural elucidation.

Beneficial effects of mushrooms on human and animals health and their nutrition

The use of mushrooms in Chinese folk medicine and the Eastern countries has been known for a long time while only in recent decades, especially in Europe, there has been interesting in studies on their effects on human health (Wasser 2014; Gru'ndemann et al. 2020). Moreover, the consumer's attention is increasingly shifting to the role that adding mushrooms to the diet can promote health and prevent the risk of disease, thanks to the effects of bioactive compounds on the human body.

In Asian countries, mushrooms have always been a primary source of food and medicine, due to the benefits they bring to physical well-being in general and the preventive and curative effects on various diseases such as cancer, cardiovascular diseases, hypertension, neuropathies, etc. Numerous studies carried out in Asian countries, and more recently also in Europe, have demonstrated the multiple effects that the different chemical components of mushrooms have on the organism, not only humans but also animals. As reported by Fernandes et al. (2015) and Cheung (2013), dietary fiber of mushrooms helps to prevent constipation, hemorrhoids, colon diseases, diabetes, and cardiovascular diseases, improves intestinal tract function and insulin and cholesterol metabolism. It also strengthens the immune system and has anti-tumor activity. But the bioactive compounds in mushrooms are numerous and varied, as well as their possible uses. Wasser (2014) suggested medicinal mushroom drugs (MM drugs) in immuno- suppressed patients.



Scheme 1 The role of mycochemicals. Partially modified from www.dreamstime.com

The antitumor MM drugs, called biological response modifiers (BRMs), are used in different types of cancer and patients undergoing chemo- and radiotherapy, improving their quality of life as they reduce side effects and help overcome cancer growth. To date, several MM products have been developed for therapeutic and commercial purposes, especially from species widespread and used in the East. The most important polysaccharides which characterize mushroom extracts are Lentinan, isolated from *Lentinula edodes* (Berk.) Pegler, Schizophyllan (Sonifilan, Sizofiran, or SPG) from *Schizophyllum commune* Fr., Ganoderan from *Ganoderma lucidum* (Curtis) P. Karst., Krestin (PSK), and PSP (polysaccharide peptide) from *Trametes versicolor* (L.) Lloyd, Grifolan from *Grifola frondosa* (Dicks.) Gray, Befungin from

Inonotus obliquus (Fr.) Pila't, and Immunoglukan P4H (pleuran) from *Pleurotus ostreatus* (Jacq.) P. Kumm. (Giavasis 2014; Wasser 2014).

The daily intake of MM as part of a healthy diet also produces beneficial effects. Food supplements such as fruit bodies powders and extracts; biomass or extracts from mycelium harvested from a submerged liquid culture in fermentation tanks or bioreactors; dried and pulverized preparations of the combined substrate, mycelium, and mushroom primordial; spores and their extracts; dried mushrooms in tablets or pills are available on the market (Wasser 2014; Reis et al. 2017).

Mushroom bioactive compounds have an enormous potential for use as performance-enhancing natural additives for livestock animals. A survey, carried out by Bonanno et al. (2019), reveals how the integration in the diet of dairy ewes of mushroom myceliated grains (a mixing of *L. edodes*, *Cordyceps* spp.,

G. lucidum, *P. ostreatus*) improves production both in terms of quantity, with a higher milk yield, and quality (less intense yellow colour of cheese, lower secondary lipid oxidation, greater oxidative stability and antioxidant content of the cheese). BederskaŁojewska et al. (2017) showed how adding edible Basidiomycetes to feed improves the productive and physiological performance of broiler chickens and laying hen. Considerable benefits are also obtained from by-products of mushroom production, which are also rich in interesting bioactive compounds for the production of beneficial animal feed, fertilizers, cosmetics, and cosmeceuticals. (He et al. 2016; Taofiq et al. 2016; Antunes et al. 2020).

Mycochemicals structures and composition

Several mycochemicals are present in mushrooms with different chemical structures and composition such as phenolic compounds, terpenoids, lipids, polysaccharides and proteins, which are easily separated from other constituents by their high molecular weights.

Phenolic compounds

The term 'phenolic compounds' includes a wide range of mycochemicals that are characterized by an aromatic ring bearing one or more hydroxyl groups. Phenolic substances are water-soluble since they most frequently occur in combination with sugar as glycosides, but also as esters and polymers. These compounds belong to different classes based on the number of phenol rings and of the functional groups linked to these moieties. Thus, a classification comprises simple phenols, phenolic acids, phenylpropanoids, flavonoids, flavonols, flavones, stilbenes, and lignans.

Phenolic acids are the main phenolic substances found in mushrooms (Ferreira et al. 2009); they are classified into two groups; hydroxybenzoic acid (HBA) and hydroxycinnamic acid (HCA). Hydroxybenzoic acid derivatives are in the bound form and are part of more complex structures as hydrolyzable tannins, lignins, sugars and organic acids. Hydroxycinnamic acid derivatives are also present mainly in the bound form, attached to cell-wall structural elements, such as lignin, cellulose, proteins or linked to organic acids, through ester bonds, such as quinic or tartaric acids (Manach et al. 2004). The most wide-spread are the HCAs, which are useful not only as providing the building blocks of lignin but also concerning disease resistance and growth regulation. Five HCAs are common, in fact almost ubiquitous in mushrooms: ferulic, sinapic, caffeic, and *p*-/*o*-coumaric acids. HCAs usually are present in mushrooms in combined form as esters; and they are obtained in best yield by mild alkaline hydrolysis, since with hot acid hydrolysis material is lost for the decarboxylation to the corresponding hydroxystirenes.

Caffeic acid occurs in mushrooms regularly as a quinic acid ester (3-*o*-caffeoylquinic, 4-*o*-caffeoylquinic, 5-*o*-caffeoylquinic). Besides, tannic and ellagic acids are observed (Ferreira et al. 2009). In mushrooms, the most prevalent HBAs derivatives are reported to be gallic, protocatechuic, gentisic, homogentisic, *p*-hydroxybenzoic, 5-sulphosalicylic, syringic, veratric, vanillic (Ferreira et al. 2009) (Table 1).

HBA and HCA compounds are derived biosynthetically from the shikimate pathway. L-phenylalanine and -tyrosine are the crucial amino acids and the building blocks in this pathway.

Flavonoids are another large group of naturally occurring phenolic compounds that are all structurally derived from the parent substance flavone consisting of two benzene rings (A and B) combined with a pyran one (C). Different classes of flavonoids are recognized, such as anthocyanidins, flavonols, flavones, isoflavones, flavanones, and flavonols (Manach et al. 2004). The flavonoids are present in nature as glycosides or aglycones.

It was reported that mushrooms do not synthesize flavonoids, however, the presence of flavonoids was found in various edible mushrooms, e.g. catechin, myricetin, chrysin, hesperetin, naringenin, naringin, formononetin, biochanin, resveratrol, quercetin, pyrogallol, rutin, and kaempferol (Gil-Ramirez et al. 2016; Ferreira et al. 2009).

Phenolic acids and flavonoids identification and quantification from some selected mushrooms [*P. ostreatus*, *P. eryngii* (DC.) Que'l., *Agaricus bisporus* (J.E. Lange) Imbach, *Cyclocybe aegerita* (V. Brig.) Vizzini, *Russula cyanoxantha* (Schaeff.) Fr., *R. virescens* (Schaeff.) Fr., *Macrolepiota procera* (Scop.) Singer, *Boletus edulis* Bull., *Lactarius deliciosus* (L.) Gray, *Coprinus comatus* (O.F. Mu"ll.) Pers., *Tuber melanosporum* Vittad.] were done by high-performance liquid chromatography coupled with mass spectrometry (HPLC–MS) (Table 1). The compounds identification derives from their retention times, their UV–Vis absorption spectra and mass spectra data and also by comparison with available data (Fogarasi et al. 2018). 4-Hydroxybenzoic acid and 5-feruloylquinic acid were found to be the major compounds in *P. ostreatus* and *A. bisporus* with concentrations of 75.042 mg/100 g-fw and 35.040 mg/100 g-fw for *P. ostreatus* and 79.50 mg/ 100 g-fw and 71.01 mg/100 g-fw for *A. bisporus*, respectively. *B. edulis* extract is characterized by high concentrations of cinnamic acid 168.614 mg/100 g-fw and catechin 145.566 mg/100 g-fw (Fogarasi et al. 2018). Hasnat et al. (2014) reported content of phenolic compounds for *R. virescens* of 8.74 and 2.21 mg gallic acid/100 g-fw, and flavonoid compounds were 2.83 and 1.02 mg catechin/100 g-fw for the water and ethanol extracts, respectively.

Among phenolic acids, the major amount of protocatechuic acid was found in *M. procera* (5.19 mg/Kg DW) (Nowacka et al. 2014). Kalogeropoulos et al. evaluated the content of individual phenolic compounds for *L. deliciosus*; *p*-OH-benzoic acid (24.5 lg/100 g fw) and *p*-OH-phenylacetic acid (18.3 lg/100 g fw) were the more abundant among the hydroxyl-benzoic acids, *o*-coumaric acid (30.2 lg/ 100 g fw) among the hydroxycinnamic acids, and chrysin (16.5 lg/100 g fw) among the flavonoids.

As concerns *C. comatus*, among the phenolic compounds, the highest content was detected for quinic acid (14.6 mg/100 g dw) and quercetin (3.01 mg/100 g fw), where the lowest amount was detected for the isoflavonoids genistein (0.023 mg/ 100 g dw) and daidzein (0.061 mg/100 g dw) (Nowakowski et al. 2020). Besides, Comatin (4, 5-Dihydroxy-2-methoxy-benzaldehyde) isolated and identified from *C. comatus* has shown hypoglycaemic properties on alloxan-induced-diabetic rats (Ding et al. 2010) (Table1).

In the literature, it is common to find the total phenolic content (TPC) found in mushrooms methanolic extract by the

Folin-Ciocalteu assay. However, this assay has some limitations since other readily oxidized compounds such as amino acids, ascorbic acid, and sugars could interfere overestimating the total phenolic content (Arbaayah and Umi 2013).

Phenolic compounds possess antioxidant properties to scavenge free radicals, to prevent lipid peroxidation, and to chelate ferrous ions (Kumar and Pandey 2013).

Table 1 Phenolic compounds of some selected mushrooms species

Mushroom species	Phenolic compounds	References
<i>Pleurotus ostreatus</i>	4-HBA, 2,4-dihydroxybenzoic acid, 4-hydroxy phenylacetic acid, pirocatechuic acid, protocatechuic acid, catechin, gallic acid, <i>o</i> -coumaric acid, cinnamic acid, 5-feruloylquinic acid, 3,5-dicaffeoylquinic acid, chlorogenic acid, syringic acid, vanillic acid, caffeic acid, ferulic acid, 2,6-dimethoxyphenol	Sarma et al. (2018), Fogarasi et al. (2018), Koutrotsios et al. (2017) and Palacios et al. (2011)
<i>Pleurotus eryngii</i>	4-HBA, <i>p</i> -coumaric acid, cinnamic acid, protocatechuic acid, gallic acid, phenol	Souilem et al. (2017) and Reis et al. (2012)
<i>Pleurotus cornucopiae</i>	Gallic acid, protocatechuic acid, chlorogenic acid, vanillin, ferulic acid, naringin, naringenin, hesperitin, formononetin, biochanin-A	Nuhu et al. (2011)
<i>Agaricus bisporus</i>	4-HBA, 2,4-dihydroxybenzoic acid, 4-hydroxy phenylacetic acid, protocatechuic acid, catechin, gallic acid, <i>p</i> -hydroxybenzaldehyde, <i>p</i> -aminophenol, catechol, coumaric acid, cinnamic acid, 4- and 5-feruloylquinic acid, 3,5-dicaffeoylquinic acid	Weijn et al. (2013), Fogarasi et al. (2018), Palacios et al. (2011)
<i>Cyclocybe aegerita</i>	Protocatechuic acid, 4-HBA, chlorogenic acid, gallic acid, caffeic acid, vanillic acid, <i>p</i> -coumaric acid, ferulic acid, sinapic acid, <i>t</i> -cinnamic acid, rutin, quercetin, kaempferol	Gasecka et al. (2016)
<i>Russula cyanoxantha</i>	Quercetin, quercetin-3- <i>o</i> -rutinoside, catechin, epicatechin	Butkhip et al. (2018)
<i>Russula virescens</i>	Catechin, ferulic acid, kaempferol, luteolin, vanillic acid, apigenin	Hasnat et al. (2014)
<i>Macrolepiota procera</i>	Protocatechuic acid	Nowacka et al. (2014)
<i>Boletus edulis</i>	4-HBA, 2,4-dihydroxybenzoic acid, gallic acid, 4-hydroxy phenylacetic acid, protocatechuic acid, caffeic acid, catechin, chlorogenic acid, gallic acid, <i>p</i> -coumaric acid, sinapic acid, <i>o</i> -coumaric acid, cinnamic acid, 3,5-dicaffeoylquinic acid, gentisinic acid, homogentisinic acid, myricetin, protocatechuic acid	Fogarasi et al. (2018) and Palacios et al. (2011)
<i>Lactarius deliciosus</i>	4-HBA, 4-hydroxy phenylacetic acid, 3,4-dihydroxy phenylacetic acid, syringic acid, vanillic acid, caffeic acid, cinnamic acid, chlorogenic acid, ferulic acid, <i>o</i> -coumaric acid, <i>p</i> -coumaric acid, tyrosol, vanillin, chrysin, kaempferol, resveratrol, gallic acid, gentisinic acid, homogentisinic acid, myricetin, protocatechuic acid, pyrogallol	Kalogeropoulos et al. (2013) and Palacios et al. (2011)
<i>Coprinus comatus</i>	Flavones, flavonols, flavanones, flavanols, biflavonoids, isoflavonoids, hydroxybenzoic acids, hydroxycinnamic acids, coumarins, chlorogenic acids	Nowakowski et al. (2020) and Cayan et al. (2018)
<i>Tuber melanosporum</i>	4,5-Dihydroxy-2-methoxy-benzaldehyde (comatin)	Ding et al. (2010)
	Homogentisic acid, 4-HBA, 3,4-dihydroxybenzaldehyde	Villares et al. (2012)
	Flavonoids, phenols	Li et al. (2019)

Terpenoids

The general term 'terpenoid' includes all such substances with a common biosynthetic origin. Terpenoids arise from the isoprene molecule $\text{CH}_2=\text{C}(\text{CH}_3)-\text{CH}=\text{CH}_2$ and their carbon skeletons originate from the union of two or more of these C5 units. Their classification is according to whether they contain two (C10), three (C15), four (C20), six (C30), or eight

(C40) such unit. Essential oils, volatile mono- and sesquiterpenes (C10 and C15), including the less volatile diterpenes (C20), the involatile triterpenoids and sterols (C30), and the carotenoids pigments (C40) are terpenoids. Each of these different classes of terpenoid is of importance in mushroom growth, metabolism, or ecology (Dewick 2009).

Chemically, terpenoids are generally lipid-soluble and are extracted from mushrooms with dichloromethane, light petroleum, or ether and can be separated by flash chromatography on silica gel or alumina using some solvents. Isomerism and the presence of different geometric conformations are common among terpenoids. It depends on the substitution around the cyclohexane ring, twisted in the so-called 'chair' form. The stereochemistry of the cyclic terpenoids is highly involved. During purification procedures, structural re-arrangement and isomerization may occur and lead to artifact formation.

Essential oils.

The mainly terpenoid essential oils include the volatile fraction responsible for the characteristic odor and scent found in many mushrooms. They are commercially important as the basis of skincare in cosmetics and flavorings in the food industry. Fogarasi et al. (2018) reported the presence of α -pinene, β - phellandrene, β -pinene, β -myrcene, and D-limonene in *A. bisporus* and *B. edulis* as main terpenoids. The in- tube extraction headspace coupled with gas chromatography-mass spectrometry (HS-ITEX/GC-MS) permits to obtain the volatile profile of selected mushrooms. The volatile constituents strongly influence the aroma profile of each mushroom variety.

Triterpenoids and sterols

Triterpenoids are compounds with a carbon skeleton based on six isoprene units. They biosynthetically derived from squalene, an acyclic C10 hydrocarbon.

They have relatively complex cyclic structures, most being either alcohols, aldehydes, or carboxylic acids. Sterols are triterpenes which are based on the cyclopentane perhydrophenantrene ring system. So, one example is ergosterol, ubiquitous in occurrence in mushrooms. Ergosterol is a component of the fungal cell membrane, which under the influence of UV irradiation is converted to vitamin D2. Besides, ergosterol shows several healthy beneficial properties such as antihyperlipidemic, anti-inflammatory, antioxidant and the effect for inhibiting fungi and bacteria growth (Koutrotsios et al. 2017).

All types of triterpenoids are isolated by very similar procedures, based mainly on column chromatography, GLC and TLC. Identities are confirmed by melting point, rotation, FT-IR, GLC-MS, and NMR experiments.

Table 2 includes the triterpenoids and sterols found in some selected mushroom species.

Different *P. ostreatus* strains were evaluated for their sterol composition. In all mushroom samples analyzed ergosterol dominated, comprising 51.9–87.4% of sterols, followed by its metabolites ergosta-7-enol (12.7%), ergosta-5,7-dienol (7.6%), and ergosta-7,22-dienol (6%) (Koutrotsios et al. 2017). The ergosterol content in *P. eryngii* was reported as 20 mg/100 g dw, although a higher value was measured in commercial samples (Souilem et al. 2017). Kikuchi et al. (2017, 2018) reported the isolation and structure elucidation of ergostane type sterols and bisabolane-type sesquiterpenes from *P. eryngii* with aromatase and nitric oxide production inhibitory effects, respectively (Table 2).

Wang et al. (2013a) reported the identification of novel and rare perhydrobenzannulated 5,5-spiroketal sesquiterpenes,

named pleurospiroketals A-E from the edible mushroom *P. cornucopiae* with inhibitory activity against nitric oxide production in lipopolysaccharide-activated macrophages with IC₅₀ values between 6.8–20.8 μ M.

From *M. procera* were isolated and identified 12 lanostane-type triterpenoids characterized by the presence of a rare '1-en-11,11-epoxy' moiety, namely lepiotaprocerins A-L. Lepiotaprocerins A-F showed significant inhibitions of nitric oxide (NO) production, while lepiotaprocerins G-L, showed cytotoxicity effects against different human cancer cell lines, and lepiotaprocerin I displayed antitubercular activity against *Mycobacterium tuberculosis* H37Ra with a MIC of 50 μ g/mL (Chen et al. 2018).

Table 2 Triterpenoids of some selected mushrooms species

<i>Pleurotus ostreatus</i>	Ergosterol, ergosta-5,7-dienol, ergosta-7-enol, ergosta-7,22-dienol, oleanolic acid, ursolic acid	Sarma et al. (2018) and Koutrotsios et al. (2017)
<i>Pleurotus eryngii</i>	Ergosterol	Souilem et al. (2017)
	Ergostane-type sterols	Kikuchi et al. (2017)
	Strophasterols E and F	Kikuchi et al. (2019)
	Bisabolane-type sesquiterpenes	Kikuchi et al. (2018)
	Eryngiolide A, pentacyclic triterpenoids	Fu et al. (2016)
<i>Pleurotus cornucopiae</i>	Ergosterol, Ergosta-5,8,22-trien-3-ol, 5,6-Dihydro-ergosterol, Ergosta-7-enol, Ergosta-7,22-dienol, Ergosta-14,22-dien-3-ol, Campesterol	Parmar and Kumar (2015)
	Pleurospiroketals A-E, Perhydrobenzannulated 5,5-spiroketal sesquiterpenes	Wang et al. (2013a)
	Monoterpenoids, sesquiterpenoids	Wang et al. (2013b)
	Ergostane-type sterols	Lee et al. (2017)
<i>Agaricus bisporus</i>	Ergosterol	Alshammaa (2017)
	Terpenoid spiro ketals	Grothe et al. (2013)
<i>Cyclocybe aegerita</i>	Bovistols A-C, Protoilludane Pasteurestin C	Surup et al. (2019)
<i>Russula cyanoxantha</i>	Ergosta-4,6,8(14),22-tetraen-3-one	Zhao et al. (2011)
<i>Macrolepiota procera</i>	Lanostane triterpenoids (Lepiotaprocerins A-L)	Chen et al. (2018)
<i>Boletus edulis</i>	Botryane sesquiterpenoids (Boledulins A-C)	Feng et al. (2011)
<i>Lactarius deliciosus</i>	Ergosterol, Ergosta-5,7-dienol, Ergosta-7-enol, Ergosta-7,22-dienol, Lanosterol, Lanosta-8,24-dienol, 4 α -Methylzymosterol	Kalogeropoulos et al. (2013)
	Azulene-type sesquiterpenoids	Tala et al. (2017)
<i>Coprinus comatus</i>	Terpenoids	Dulay et al. (2015)
<i>Tuber magnatum</i>	Ergosterol, Ergosta-7,22-dienol, Ergosta-5,8-dien-3-ol, Brassicasterol, 5-Dihydroergosterol, Campesterol, 24(28)-Dehydroergosterol, Barrigenol R1, Fungisterol, Lanosterol, Dehydroepiandrosterone	Tejedor-Calvo et al. (2020) and Yeh et al. (2016)
<i>Tuber melanosporum</i>	Ergosterol, Ergosta-7,22-dienol, Brassicasterol, 5-Dihydroergosterol, Campesterol, 24(28)-Dehydroergosterol, Barrigenol R1, Fungisterol, Lanosterol, β -Sitosterol, Dehydroepiandrosterone	Tejedor-Calvo et al. (2020) and Yeh et al. (2016)
<i>Tuber borchii</i>	Ergosterol, Ergosta-7,22-dienol, Brassicasterol, Campesterol, 24(28)-Dehydroergosterol, Dehydroepiandrosterone	Tejedor-Calvo et al. (2020) and Yeh et al. (2016)

Three non-isoprenoid botryane sesquiterpenoids, named boledulins A-C were isolated from the cultures of *B. edulis* Bull. with moderate inhibitory activity against five human cancer cell lines (Feng et al. 2011), while from the edible mushroom *L. deliciosus*, azulene-type sesquiterpenoids were characterized (Tala et al. 2017).

Many sterols such as campesterol, lanosterol, brassicasterol, β -sitosterol, ergosterol were analyzed in the fruiting bodies

of different *Tuber* species (Table 2). The main sterols found in *Tuber magnatum* Picco and *T. melanosporum* fruiting bodies were ergosterol and brassicasterol, which amounted to 63.1–66.7% and 15.7–21.3% of the total sterols, respectively. Also the mycelia of *T. borchii* Vittad. are a rich source of ergosterol (90.3%). The complex composition profile of the truffle sterols might be taken as the fingerprint for the identification of the truffle species (Yeh et al. 2016).

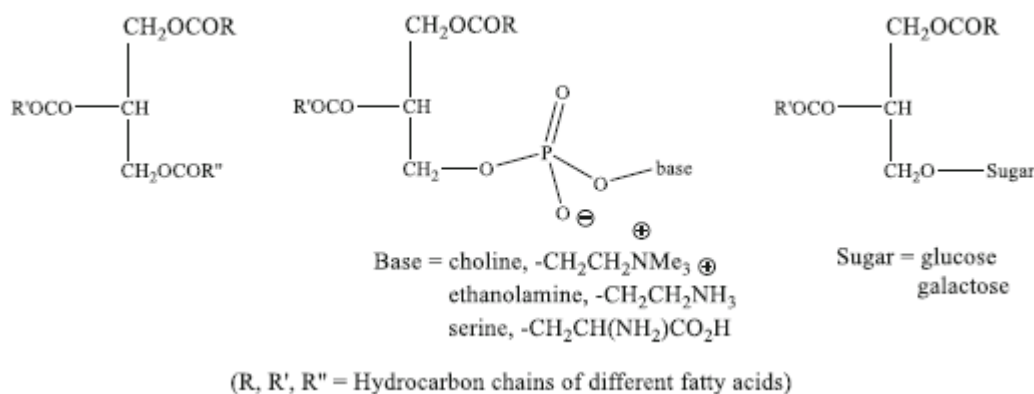


Fig. 1 Chemical structures of mushroom lipids

Fatty acids and lipids

Mushrooms are an essential source of fatty acids that occur mainly in bound form, esterified to glycerol, as fats or lipids. They are crucial as membrane constituents in the mitochondria and chloroplasts and provide mushrooms with a storage form of energy. The content of total lipids ranges mostly from 1 to 4% of the dry weight. Besides, mushroom fats are rich in unsaturated fatty acids (PUFA) and particularly in linoleic acid (Koutrotsios et al. 2017).

Lipids are known by their distinct solubility properties and are extracted with alcohol, ether or dichloromethane from mushrooms.

The general structures for the three main classes of mushrooms lipids are reported in Fig. 1.

Structural variation within each class is due to the different fatty acid residues that may be present. The identification of lipids mainly requires the determination of their fatty acid components. Fatty acids are determined as methyl esters (FAMES) after hot saponification of the sample, followed by reaction with BF₃/MeOH. The resulting FAMES are analyzed by GC–MS by comparison with standard FAMES and confirmed utilizing mass spectra library (Helrich 1990).

In some selected mushrooms species, the fatty acid composition is characterized by a prevalence of polyunsaturated linoleic acid (C18:2ω6), monounsaturated oleic acid (C18:1ω9), and saturated palmitic acid (C16:0) (Table 3). The fatty acids are divided into saturated (SFA), monounsaturated (MUFA), and polyunsaturated (PUFA). In particular, the ratio between the single components of PUFA is fundamental in preventing cardiovascular diseases. PUFAs are a family of so-called 'essential' fatty acids that are converted to tissue hormones useful to prevent blood clotting and hypertension (Pietrzak-Fiećko et al. 2016).

Koutrotsios et al. (2017) evaluated the fatty acid profile of different *P. ostreatus* strains, collected in Greece, including saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), ω3 and ω6 fatty acids. PUFA was the major fatty acid class detected; linoleic acid (C18:2ω6) dominated in all samples (56.8–80.5%) followed by oleic (C18:1ω9) and palmitic (C16:0) (6.3–19.5 and 7.5–12.1%, respectively) (Table 3).

Jing et al. (2012) reported a selective method where fatty acids from cultivated mushrooms *P. eryngii*, *C. aegerita* and *C. comatus* were derivatized with BAETS as the labeling reagent and identified by high-performance liquid chromatography with fluorescence detection and online mass spectrometry (HPLC-FLD-MS/MS).

Total fatty acids (TFAs) values for *P. eryngii*, *C. aegerita* and *C. comatus* (dw) were 42.60, 48.95, and 79.21 mg 10 g⁻¹ respectively, while UFA:SFA ratio were 3.23, 3.29, and 3.03, respectively. Linoleic (C18:2 ω 6) and oleic (C18:1 ω 9) acids were the main FA found and their content was between 27.17–49.34 mg 10 g⁻¹ and 4.08–22.15 mg 10 g⁻¹, respectively.

Table 3 Fatty acids of some selected mushrooms species

<i>Pleurotus ostreatus</i>	SFA, MUFA, PUFA, n – 6, n – 3	Koutrotsios et al. (2017) and Fogarasi et al. (2018)
<i>Pleurotus eryngii</i>	SFA (C10:0, C11:0, C12:0, C13:0, C14:0, C15:0, C16:0, C17:0, C18:0, C19:0, C20:0, C21:0, C22:0), MUFA (C16:1 ω 7, C16:1 ω 9, C18:1 ω 9), PUFA (C18:2 ω 6, C18:3 ω 3, C20:4 ω 6, C22:6 ω 3)	Jing et al. (2012) and Rodrigues et al. (2015)
<i>Pleurotus cornucopiae</i>	SFA (C14:0, C15:0, C16:0, C17:0, C18:0, C20:0, C24:0), MUFA (C16:1 ω 7, C16:1 ω 9, C18:1 ω 9), PUFA (C18:2 ω 6, C18:3 ω 3, C20:4 ω 6, C22:6 ω 3)	Rodrigues et al. (2015)
<i>Agaricus bisporus</i>	SFA, MUFA, PUFA, C16:1 ω 7, C16:0, C18:0, C18:1 ω 9, C18:2 ω 6, C20:0	Sande et al. (2019) and Fogarasi et al. (2018)
<i>Cyclocybe aegerita</i>	SFA (C10:0, C11:0, C12:0, C13:0, C14:0, C15:0, C16:0, C17:0, C18:0, C19:0, C20:0, C21:0, C22:0), MUFA (C16:1 ω 7, C16:1 ω 9, C18:1 ω 9), PUFA (C18:2 ω 6, C18:3 ω 3, C20:4 ω 6, C22:6 ω 3)	Jing et al. (2012)
<i>Russula cyanoxantha</i>	SFA (C6:0, C8:0, C10:0, C12:0, C13:0, C14:0, C15:0, C16:0, C17:0, C18:0, C20:0, C21:0, C22:0, C23:0, C24:0), MUFA (C16:1, C18:1 ω 9, C20:1, C24:1), PUFA (C18:2 ω 6, C18:3 ω 3, C20:2, C20:3 ω 3, C20:5 ω 3)	Grangeia et al. (2011)
<i>Russula virescens</i>	SFA (C16:0, C18:0), MUFA (C18:1 ω 9), PUFA (C18:2 ω 6)	Leal et al. (2013)
<i>Macrolepisma procera</i>	SFA (C16:0, C18:0), MUFA (C18:1 ω 9), PUFA (C18:2 ω 6)	Yılmaz et al. (2013)
<i>Boletus edulis</i>	SFA (C6:0, C8:0, C10:0, C12:0, C14:0, C15:0, C16:0, C17:0, C18:0, C20:0, C22:0, C23:0, C24:0), MUFA (C16:1, C17:1, C18:1 ω 9, C20:1, C22:1 ω 9, C24:1), PUFA (C18:2 ω 6, C18:3 ω 3, C18:3 ω 6, C20:2, C20:4 ω 6, C20:3 ω 3 + C21:0, C20:5 ω 3)	Heleno et al. (2011) and Pietrzak-Fiećko et al. (2016)
<i>Lactarius deliciosus</i>	SFA (C10:0, C11:0, C12:0, C13:0, C14:0, C15:0, C16:0, C17:0, C18:0, C20:0, C21:0, C23:0, C24:0), MUFA (C16:1 ω 9, C16:1 ω 7, C18:1 ω 9, C20:1 ω 9), PUFA (C18:2 ω 6, C18:3 ω 3, C20:2 ω 6, C20:3 ω 6, C20:4 ω 6 + C22:0, C20:3 ω 6, C20:5 ω 3, C22:2 ω 6)	Kalogeropoulos et al. (2013) and Ergönül et al. (2012)
<i>Coprinus comatus</i>	SFA (C10:0, C11:0, C12:0, C13:0, C14:0, C15:0, C16:0, C17:0, C18:0, C19:0, C20:0, C21:0, C22:0), MUFA (C16:1 ω 7, C16:1 ω 9, C18:1 ω 9), PUFA (C18:2 ω 6, C18:3 ω 3, C20:4 ω 6, C22:6 ω 3)	Jing et al. (2012) and Ergönül et al. (2012)
<i>Tuber melanosporum</i>	SFA (C14:0, C15:0, C16:0, C17:0, C18:0, C20:0, C21:0, C22:0, C23:0, C24:0), MUFA (C16:1, C17:1, C18:1 ω 9, C20:1 ω 9, C22:1 ω 9, C24:1 ω 9), PUFA (C18:2 ω 6, C20:2, C20:4 ω 6, C22:6 ω 3)	Jiang et al. (2018)

SFA saturated fatty acids, MUFA monounsaturated fatty acids, PUFA polyunsaturated fatty acids

Also for *P. cornucopiae* the linoleic acid (C18:2 ω 9) was the main FA, with a composition characterized by a higher content of mono (MUFA) and polyunsaturated FA (PUFA) than of saturated FA (SFA) (Rodrigues et al. 2015).

The lipids analyzed for *A. bisporus* showed a high content of unsaturated acids with linoleic acid (C18:2 ω 6) as the main constituent of fruiting bodies (33.3%) and stems (39.4%). The total saturated fatty acid (SFA) content was between 22.1 and 26.5% of total lipids, palmitic acid (C16:0) was the major SFA at about 14% followed by stearic acid (C18:0) at about 4%. Oleic acid (C18:1 ω 9) was the major monounsaturated fatty acid (MUFA) present at about 1.5% of total lipids (Sande et al. 2019).

As concerns *R. cyanoxantha* the major fatty acid found was linoleic acid (C18:2 ω 6) (43.65%) followed by oleic acid (C18:1 ω 9) (28.39%) and palmitic acid (C16:0) (12.95%) (Grangeia et al. 2011).

The fatty acid composition of different wild *Boletus* species collected in Portugal was reported by Heleno et al. (2011). (Table 3). The major fatty acid found in

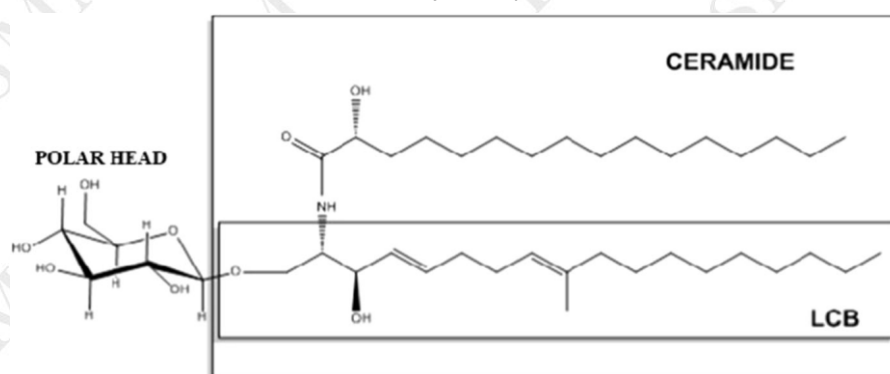


Fig. 2 Chemical structure of mushroom glycosphingolipids

A. edulis was oleic acid (C18:1 ω 9) (42.5%) followed by linoleic acid (C18:2 ω 6) (41.32%) and palmitic acid (C16:0) (9.57%). A very similar profile of fatty acid composition was reported for 33 samples of wild *B. edulis* in the form of caps and stems, collected from selected regions of Poland. The dominant fatty acids in all samples analyzed were C18:2 ω 6, C18:1 ω 9, and C16:0 (Pietrzak-Fiećko et al. 2016).

Kalogeropoulos et al. (2013) reported the fatty acid composition of wild *L. deliciosus* from Greece. The prevalent fatty acids were linoleic acid (C18:2 ω 6) (31.78%), followed by stearic acid (C18:0) (29.83%) and oleic acid (C18:1 ω 9) (21.82%) (Table 3).

Another class of lipids found in mushrooms is glycosphingolipids (GLSs) and the cerebroside in particular. A polar head (usually a monosaccharide or a carbohydrate chain) and a fatty acyl group are linked to a long-chain aminoalcohol called a long-chain base (LCB). The fatty acyl chain is amide-linked to the LCB and together they make up the ceramide; the monosaccharide or oligosaccharide group is linked to the primary alcoholic function of the ceramide (Fig. 2).

GLSs are ubiquitous membrane constituents of mushrooms and are believed to possess a wide range of biological activities, including modulation of growth and regulation of differentiation. They are involved in membrane phenomena, such as cell–cell recognition, cell–cell adhesion, antigenic specificity, and other kinds of transmembrane signaling.

β -Glucosylceramide is by far the most common GLS from mushrooms. A peculiarity of glucosylceramides from mushrooms is the frequent occurrence of a di-unsaturated C18 sphingosine with a methyl branching at C-9. Structure determination was based on carbohydrate analysis, methylation analysis, chemical degradation, and extensive use of FAB-MS (Itonori et al. 2004). Three cerebroside with different lengths of the fatty acid portion have been isolated and identified from *Pleurotus cornucopiae* (Paulet) Rolland (Lee et al. 2017). Furthermore, purified acidic glycosphingolipids (AGLs) from *P. eryngii* were reported to induce interleukin-2 (IL-2) release from invariant natural killer T (iNKT) cells inducing prolonged retention of IL-4 in serum in vitro and in vivo (Fu et al. 2016). So through iNKT cell activation AGLs isolated from *P. eryngii* might be involved in the maintenance of immunohomeostasis. An important secondary metabolite from mushrooms is lovastatin, a polyketide employed as a cholesterol-lowering drug that inhibits (3S)-hydroxy- 3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This is a key enzyme in the synthesis of mevalonate, since it is the immediate precursor of cholesterol and lovastatin is the lead compound of all of the drugs classified as statins.

Lovastatin was discovered from *Aspergillus terreus* and *Monascus ruber* in the 1970s and is a natural product in oyster mushrooms (Chen et al. 2012) (Fig. 3).

Polysaccharides

Mushrooms are a significant source of polysaccharides. The structural complexity of polysaccharides is ascribed to the linkage between two sugar units, through an ether linkage, in several different ways. The reducing end of one sugar (C1) can condense with any hydroxyl group of a second sugar (at C2, C3, C4, or C6) so that during polymerization some sugars may be substituted in two positions, leading to branched chains structures. Besides, the ether linkage can have either a α - or β -configuration, due to the stereochemistry of simple sugars, and both kinds of linkage can co-exist in some molecule.

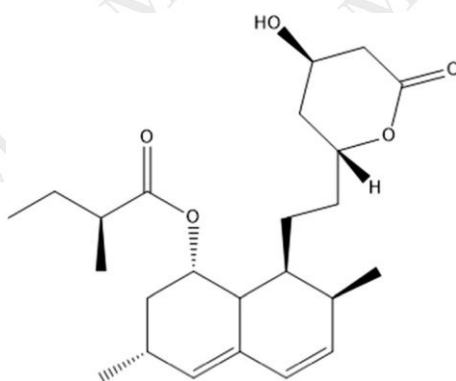


Fig. 3 Chemical structure of lovastatin

Generally, the polysaccharides are present in the mushroom cell wall and include α -glucans and β -glucans. These macromolecules are composed of glucopyranose units linked with glycosidic bonds of the type (1 \rightarrow 6)- β , (1 \rightarrow 3)- β , or (1 \rightarrow 3)- α . Mushrooms are characterized by different kinds of polysaccharides that include not only glucans but also heteroglycans and proteoglycan classes. Polysaccharides that include residues of only one type of monosaccharide unit are known as homoglycans, while residues of two or more types of monosaccharide molecules are categorized as heteroglycans (Kozarski et al. 2014).

As concerns, the extraction and purification procedures, usually the polysaccharides are isolated by successive hot-water extractions followed by ethanol precipitation. Chromatographic methods such as size-exclusion (SEC) and ion-exchange chromatography (IEC) are used as purification procedures of the crude polysaccharides, while chemical reactions of hydrolysis and derivatization together with NMR experiments are useful in providing information for their structural elucidation (Sun et al. 2010a).

Polysaccharides isolated and identified from mushrooms differ in their physical-chemical properties such as in their water solubility, molecular weight, size of the molecule, and structure (Table 4). Recently, polysaccharides isolated from mushrooms have attracted increasing attention for their wide spectrum of biological properties, such as antioxidative, antitumor, immunomodulation (BRMs), and anti-inflammatory effects (Selvamani et al. 2018). The major pharmaceutical properties of mushrooms, i.e. antitumor activities and immunity potentiation, are ascribed to β -glucans. Many fungal β -glucans stimulate both innate and adaptive immunity. They activate innate immune system components such as natural killer (NK) cells, neutrophils, macrophages, and cytokines. These cytokines, in turn activate adaptive immunity with the stimulation of B-cell for antibodies production and promotion of T-cell differentiation to T-

helper cells, which mediate cell and humoral immunities (Oloke and Adebayo 2015).

Pleuran, a water soluble polysaccharide [β -(1,3/ 1,6)-D-Glucan], is the best-known β -glucan isolated from *P. ostreatus* with a molecular weight of 762 KD. It is composed of a backbone (1 \rightarrow 3) linked β -D- glucose with a side chain of a β -(1 \rightarrow 6) or β -(1 \rightarrow 4)-D-glucosyl residue of ever fourth glucose unit. The compound exhibit anti-neoplastic properties against different cells, including breast cancer MCF-7, prostate cancer cells PC-3 and colorectal HT-29 cancer cells. It possesses also antiviral and antioxidative properties (Golak-Siwulska et al. 2018).

The purified polysaccharides PEPE-A1 and PEPE- A2 from *P. eryngii* are characterized by a β -(1 \rightarrow 3)- glucan as the backbone accompanied by α -(1 \rightarrow 6)-D- glucosyl residues side chains. They showed a strong inhibitory effect on lipid accumulation (Fu et al. 2016). Recently, a mannogalactan with the main chain of (1 \rightarrow 6)-linked- α -D-galactopyranosyl and 3-O- methyl- α -D-galactopyranosyl residues, both partially substituted at OH-2 by β -D-Manp units was isolated from *P. eryngii* and tested against murine melanoma cells (Biscaia et al. 2017).

Zhang et al. (2014) isolated three subfractions of intracellular zinc polysaccharides (IZPS) from *P. cornucopiae*. All the subfractions have shown antioxidant activities in vitro and in vivo. They were found able to act as upregulation of the superoxide dismutase, GSH peroxidase and catalase, and significantly decreased the contents of malondialdehyde and lipid peroxidation in vivo. PCPS from *P. cornucopiae* mushroom extract is a β -(1 \rightarrow 6)-glucan possessing a proinflammatory effect on innate immune cells (Minato et al. 2017).

From *A. bisporus* a new heteropolysaccharide consisting of ribose, rhamnose, arabinose, xylose, mannose, glucose, and galactose with 1 \rightarrow 2 and 1 \rightarrow 4 glycosidic bonds and probably 1 \rightarrow 3 glycosidic bonds was isolated and identified with high in vitro immunobiological activity (Liu et al. 2020a, b, c).

Motoshima et al. (2018) identified a fucogalactan from *C. aegerita* (FG-Aa) characterized by (1 \rightarrow 6)- linked α -D-galactopyranosyl main chain, substituted at O-2 by non-reducing end units of α -L-Fucp, on the average of one to every second residue of the backbone. The obtained fucogalactan was evaluated against arginase from *Leishmania amazonensis*.

A water-insoluble (1 \rightarrow 3)- β -D-Glucan was firstly isolated from the fresh fruiting bodies of *R. virescens*, and then the sulfated derivative was synthesized with sulfur trioxide-pyridine complex. The sulfated derivative exhibited enhanced anti-tumor activities against Sarcoma 180 tumor cell (Li et al. 2020). Besides, a water-soluble polysaccharide (RVP) with anti-oxidant properties was isolated from the fruiting bodies of *R. virescens* consisting of (1 \rightarrow 6)-linked- α -D-galactopyranosyl and (1 \rightarrow 2,6)-linked- α -D-galactopyranosyl residues that terminated in a single non- reducing terminal (1 \rightarrow)- α -D-mannopyranosyl residue at the O-2 position of each (1 \rightarrow 2,6)-linked- α -D- galactopyranosyl residues along the backbone (Sun et al. 2010a). Also RVP was sulfated and in vitro activity test data indicated that the SRVPs showed better antioxidant, anticoagulant, antitumor and antibacterial activities compared with RVP.

Three crude polysaccharides (BEPF30, BEPF60, and BEPF80) were isolated from the fruiting bodies of *B. edulis* and investigated for their antioxidant activities. BEPF60 showed significant reducing power and chelating activity together with the highest inhibitory effects on hydroxyl and superoxide radicals (Zhang et al. 2011). Other crude water-soluble polysaccharides (BEBPs) were extracted from *B. edulis* and evaluated for their antioxidant activities. BEBP-3 showed a significant anti-oxidant activity (Luo et al. 2012).

Table 4 Polysaccharides of some selected mushrooms species

Mushrooms species	Polysaccharides	References
<i>Pleurotus ostreatus</i>	Pleuran [β -(1,3/1,6)-D-Glucan] α -(1 \rightarrow 3)-glucans	Selvamani et al. (2018) Golak-Siwulska et al. (2018)
<i>Pleurotus eryngii</i>	Mycelium polysaccharides 2 (POMP2), POPS-1 PEPE-A1, PEPE-A2	Sarma et al. (2018) Fu et al. (2016)
<i>Pleurotus cornucopiae</i>	Partially methylated mannogalactan Intracellular zinc polysaccharides (IZPS)	Biscaia et al. (2017) Zhang et al. (2014)
<i>Agaricus bisporus</i>	β -glucan (PCPS) [β -(1 \rightarrow 6)-Glucan] β -glucan [β -(1 \rightarrow 6)-Glucan], mannogalactan	Minato et al. (2017) Smiderle et al. (2011)
<i>Cyclocybe aegerita</i>	Heteropolysaccharide ABP 1a Fucogalactan (FG-Aa)	Liu et al. (2020a, b, c) Motoshima et al. (2018)
<i>Russula cyanoxantha</i>	Ac-MPS, AI-MPS	Jing et al. (2018)
<i>Russula virescens</i>	β -glucan (1 \rightarrow 3)- β -D-glucan, RVP	Butkhup et al. (2018) Sun et al. (2010b)
<i>Macrolepiota procera</i>	SRVPs	Li et al. (2020)
<i>Boletus edulis</i>	Polysaccharides Polysaccharides (BEBP-1, BEBP-2 and BEBP-3)	Nowak et al. (2018) Luo et al. (2012)
<i>Lactarius deliciosus</i>	Polysaccharids (BEPF30, BEPF60 and BEPF80) Polysaccharide (LDG-M) Polysaccharide (LDG-A) Polysaccharide (LDG-B) Polysaccharide (LDGO-A)	Zhang et al. (2011) Su et al. (2019) Hou et al. (2019) Hou et al. (2016) Ding et al. (2015)
<i>Coprinus comatus</i>	Modified polysaccharide (MPCC) Polysaccharide (CCPP-1) Polysaccharide (CC30w-1)	Zhao et al. (2019) Liu et al. (2013) Zhou et al. (2013)
<i>Tuber magnatum</i>	(1 \rightarrow 3)- β -D-glucan (1 \rightarrow 3)- β -D-glucan	Tejedor-Calvo et al. (2020) Tejedor-Calvo et al. (2020)
<i>Tuber melanosporum</i>	Exo-polysaccharides (TP1, STP1, STP2)	Liu et al. (2020a, b, c)
<i>Tuber borchii</i>	(1 \rightarrow 3)- β -D-glucan	Tejedor-Calvo et al. (2020)

Lactarius deliciosus is an important source of polysaccharides. Su et al. (2019) reported the structural characterization and immune regulation activity of a novel polysaccharide (LDG-M) from *L. deliciosus* Gray. LDG-M was composed of β -D-glucose and α -D-lyxose with ratio 2:1. The proposed structure of LDG-M was a backbone of 1,6-linked- β -D-glucose and 1,4,6-linked- β -D-glucose, with branches composed of one (1 \rightarrow 4)-linked- α -D-lyxose residue (Table 4). The structural elucidation of LDG-A indicated a backbone of 1,6-disubstituted- α -L-mannopyranose with branches at O-2 mainly composed of a (2 \rightarrow 3)- α -D-xylopyranose residue. LDG-A exhibited marked antitumor activities in vivo. A new heteropolysaccharide (LDG-B) with a backbone of (1,6)-linked-D-galactose and (1,2,6)-linked-D-galactose with branches composed of 4-linked-D-glucose and 6-linked-D-galactose residue was identified from *L. deliciosus*. Cell cycle test data showed that LDG-B could promote the proliferation of B cells and macrophage cells by affecting G0/G1, S and G2/M phases (Hou et al. 2016). Besides, also the structure elucidation and anti-tumor activity of water-soluble oligosaccharides (LDGO-A) were reported by Ding et al. (2015).

A modified polysaccharide named MPCC was obtained by snailase hydrolysis from *C. comatus* with antioxidant and hepatoprotective properties (Zhao et al. 2019). The structural investigation of CCPP-1 from *C. comatus* has shown that CCPP-1 was α -D-(1 \rightarrow 4)-glucan with branches at C-6 consisting of non-reducing terminal approximately every fourteen residues. While the crude polysaccharide fractions CCPP showed significant hypoglycemic activity, CCPP-1 was not

useful on reducing blood sugar (Liu et al. 2013).

As concerns *Tuber* fruiting bodies and fermentation system, the structure, the physicochemical and biological properties of the polysaccharides have not been thoroughly investigated. Tejedor-Calvo et al. (2020) reported a preliminary screening of the main bioactive compounds for *T. magnatum*, *T. melanosporum* and *T. borchii* by using pressurized liquid extractions (PLE). The polysaccharide composition of the obtained extracts was investigated by NMR analysis and their immunomodulatory activity tested in vitro with cell cultures. NMR investigation revealed that the extracted polysaccharides were β -(1 \rightarrow 3)-glucans and a heteropolymer consisting of galactose and mannose.

Proteins, peptides and lectins

Other macromolecular mycochemicals isolated from mushrooms with high molecular weight are proteins, peptides, and lectins.

The proteins in mushrooms, as in other plants, are high molecular weight polymers of amino acids. The amino acids are arranged in a particular linear order and each protein has a specific amino acid sequence. Proteins are usually purified according to molecular weight so they are subjected to gel filtration on a column of Sephadex. Separation of proteins by gel electrophoresis is also partly determined by their molecular size since their mobility on the gel is closely related to their charge properties (Oloke and Adebayo 2015).

The composition of mushroom proteins seems to be of higher nutritional value concerning most plant proteins. Mushrooms proteins contain all nine essential amino acids required by humans and can be used as a substitute for meat (Kakon et al. 2012). High contents of proteins 38.9 and 36.9% were observed in

A. bisporus and *B. edulis*, respectively (Nagy et al. 2017). Mushrooms are a rich source of proteins with several properties for biotechnological and medicinal applications. Immunomodulatory proteins (FIPs) are a group of fungal proteins able to alter the cytokine response (Oloke and Adebayo 2015). Proteins isolated from selected mushrooms exhibited antiviral, antitumor, antifungal, and antibacterial properties (Table 5). Moreover, the fruiting bodies and mycelium of several mushrooms are an abundant source of ergothioneine, an unusual sulfur-containing derivative of histidine, with antioxidant properties (Chen et al. 2012).

Many proteins are also enzymes, catalyzing particular steps in either primary or secondary metabolism, and possess health-promoting effects. Laccases were isolated from *P. ostreatus* and *P. cornucopiae* with antiviral effect against the hepatitis C virus and HIV-1 reverse transcriptase, respectively (Table 5). Lectins are another group of mycochemicals that include polysaccharide-protein and polysaccharide-peptide complexes. Lectins derived from mushrooms exhibit antiproliferative, immunomodulatory, antitumor, HIV-1 reverse transcriptase inhibiting, cell growth- regulating, and many more properties (Oloke and Adebayo 2015). Some proteins, peptides, and lectins isolated from various selected mushrooms are reported in Table 5.

From *P. ostreatus* a Cibacron blue affinity-purified protein (CBAEP) was isolated with potent antitumor, anticancer and immunomodulatory activity against Sarcoma-180, Dalton lymphoma (DL)-bearing mice, and B16FO melanoma tumor-bearing mice (Sarma et al. 2018).

Table 5 Proteins, peptides and lectins of some selected mushrooms species

Mushrooms species	Proteins, peptides and lectins	References
<i>Pleurotus ostreatus</i>	Cibacron blue affinity purified protein (CBAEP)	Sarma et al. (2018)
	Pleurostrin	Erjavec et al. (2012)
	Dimeric lectin	Oloke and Adebayo (2015)
	Laccase	Golak-Siwulska et al. (2018)
<i>Pleurotus eryngii</i>	Concanavalin A	Sarma et al. (2018)
	Eryngin	Erjavec et al. (2012)@
	Laccase	Fu et al. (2016)
	Protease (Pleureryn)	Fu et al. (2016)
<i>Pleurotus cornucopiae</i>	PEP 1b	Hu et al. (2018)
	Oligopeptides	Golak-Siwulska et al. (2018)
	Laccase	Wu et al. (2014)
	Lectin (PCL-M)	Oguri (2020)
<i>Agaricus bisporus</i>	Lectin (ABL)	Verma et al. (2019)
	Protein FIIb-1	Verma et al. (2019)
<i>Cyclocybe aegerita</i>	Ribotoxin-like protein (Ageritin)	Citores et al. (2019)
	Lectin (AAL)	Liu et al. (2017)
	Lectin (AAL-2)	Ren et al. (2015)
<i>Russula virescens</i>	Laccase	Zhu et al. (2013)
	Feruloyl esterase (FAE)	Wang et al. (2014b)
<i>Macrolepiota procera</i>	β -Trefoil lectin (MPL)	Žurga et al. (2017)
<i>Boletus edulis</i>	β -Trefoil lectin (BeL)	Žurga et al. (2017)
<i>Lactarius deliciosus</i>	Laccase	Khaund and Joshi (2014)
<i>Coprinus comatus</i>	Protein Y3	Nowakowski et al. (2020)
	Laccases	Nowakowski et al. (2020)
<i>Tuber borchii</i>	Lectin (Cyanovirin-N)	Matei et al. (2011)

Besides, pleurostrin and eryngin are two proteins isolated from *P. ostreatus* and *P. eryngii* mushrooms with antibacterial and antifungal properties (Erjavec et al. 2012). The laccase isolated from *P. ostreatus* exhibited an antiviral effect against the hepatitis C virus (Golak-Siwulska et al. 2018). A dimeric lectin, composed of subunits with a molecular weight of 40 and 41 KDa, isolated from fresh fruiting bodies of *P. ostreatus* exerted antitumor activity in mice bearing sarcoma S-180 and hepatoma H-22 (Table 5).

Fu et al. (2016) reported the isolation of a laccase from *P. eryngii* with antiviral activity against HIV. The laccase was active against HIV-1 growth with an IC₅₀ of 2.2 μ M by inhibiting HIV-1 reverse transcriptase. Also a protease named pleureryn, extracted from fresh fruiting bodies of *P. eryngii*, showed (23.1 \pm 0.6)% and (91.4 \pm 3.2)% inhibition of HIV-1 reverse transcriptase at 3 and 30 mM, respectively (Table 5).

Hu et al. (2018) reported the functional characterization of a *P. eryngii* protein (PEP 1b). PEP 1b is an immunomodulatory protein with 21.9 KDa able to induce the M1-polarization of the macrophage cell line RAW 264.7 cells through the

activation of the TLR4-NF- κ B and MAPK signal pathways.

Two types of angiotensin I-converting enzyme (ACE) inhibitory oligopeptides were obtained from the basidioma of *P. cornucopiae*. The amino acid sequences of the two purified oligopeptides were found to be RLPSEFDLSAFLRA and RLSGQTIEVTSEYLFRH. Besides, from the fermentation broth of *P. cornucopiae* was isolated a new laccase with a molecular mass of 67 KDa. It inhibited proliferation of the hepatoma cells HepG2, the breast cancer cells MCF-7, and the activity of HIV-I reverse transcriptase with IC50 values of 3.9, 7.6 and, 3.7 μ M, respectively (Wu et al. 2014). Besides, a divalent cation-dependent GalNAc-specific lectin (PCL-M) was purified from the mycelia of *P. cornucopiae*. It is a multimeric glycoprotein composed of 40 KDa subunits linked by disulfide bonds (Oguri 2020).

A lectin, isolated from *A. bisporus* (ABL) showed antiproliferative effects on different cell types and might be useful for glaucoma. Besides, the fruiting bodies of *A. bisporus* are associated with a protein, named FIIb-1, characterized as tyrosinase (Verma et al. 2019).

Recently, a ribotoxin-like protein, named Ageritin was isolated from the basidiomycetes *C. aegerita*. Several biological activities are ascribed to Ageritin such as antibacterial, antiviral, endonuclease, nuclease, antifungal, and cytotoxicity to COLO 320, HeLa and, Raji cells by promoting apoptosis (Citores et al. 2019). The lectin (AAL), isolated from *C. aegerita* exhibited antitumor activity by inducing apoptosis (Liu et al. 2017), while lectin-2 (AAL-2) and its complexes with GlcNAc and GlcNAcb1-3Gal b1- 4GlcNAc revealed the structural features of specific recognition of non-reducing terminal N-acetylglucosamine (Ren et al. 2015).

A novel laccase was purified and characterized by *R. virescens*. Its N-terminal amino acid sequence was AIGPTAELVV and it was able to degrade various phenolic compounds and to decolorize several dyes (Zhu et al. 2013).

Z̃ urga et al. (2017) isolated novel ricin B-like lectin with a b-trefoil fold from *M. procera*, designated as MpL with nematocidal activity indicating a function in protecting fruiting bodies against parasites. MpL was studied for potential delivery of peptidase protein inhibitors to lysosomes showing that it is a promising carrier of protein drugs to intracellular targets.

An antiviral protein Y3 isolated from *C. comatus* showed an inhibitory effect on the tobacco mosaic virus. Y3 has shown anticancer potential inducing caspase-dependent apoptosis in Jurkat cells of human T-cell leukemia. Besides, also laccases from mycelia of *C. comatus* have shown antiproliferative and antiviral properties (Nowakowski et al. 2020) (Table 5).

(To be continued)

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Aiming to build the relationship between the members and the Society, the publication of the newsletters was proposed before the launching of the Society. The newsletters represent one of the key official publications from the Society. Contents of the newsletters will include notifications of the decisions made by the committee board, reviews or comments contributed by ISMM committee members, conferences or activities to be organized, and the status updated in research, industrialization, and marketing for medicinal mushrooms. The newsletters will be released quarterly, by the first Monday of every January, April, July, and October, with possible supplementary issues as well. The Newsletter is open to organizations or professionals to submit news, comments, or scientific papers relating to medicinal mushroom research, marketing, or industry.

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